

Research Article

Effective syntheses of 2-trimethylsilylmethyl-3-trimethylsilyl-1-propene and its 1,1-*d*₂- and 1,1,1',1',3,3- *d*₆-isotopomers[†]

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Summary

New and effective routes to synthesize 2-trimethylsilylmethyl-3-trimethylsilyl-1-propene and its 1,1-*d*₂- and 1,1,1',1',3,3-*d*₆-isotopomers have been developed, using the displacement reaction of lithium trimethylsilylcyanocuprate with allylic halides and tosylates. These compounds are pivotal precursors for the gas-phase synthesis and characterization of the trimethylenemethane anion, and for negative ion photoelectron spectroscopic investigations of the singlet–triplet splitting in trimethylenemethane. Copyright © 2001 John Wiley & Sons, Ltd.

Key Words: 2-trimethylsilylmethyl-3-trimethylsilyl-1-propene; trimethylsilylmethyl-2-propen-1-ol; trimethylenemethane; regiospecific deuterium label

Introduction

2-Trimethylsilylmethyl-3-trimethylsilyl-1-propene (**1**) is a necessary precursor for the gas-phase synthesis of the negative ion of trimethylenemethane.¹ This ion is required for measurements of the electronic affinity and singlet–triplet splitting of trimethylenemethane by negative ion photoelectron spectroscopy. In order to elucidate the regioselectivity

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and mechanism of ion formation, the 1,1- d_2 -2-trimethylsilylmethyl-3-trimethylsilyl-1-propene (d_2 -**1**) has been produced and used in generating 1,1- d_2 -trimethylenemethane anion. The 1,1,1',1',3,3- d_6 -2-trimethylsilylmethyl-3-trimethylsilyl-1-propene (d_6 -**1**) is also needed for aid in the interpretation of vibrational fine structures in the negative ion photoelectron spectrum of the trimethylenemethane anion.^{2,‡} The significance of these compounds is not limited to our purposes alone. Allylsilanes are versatile synthetic reagents and trimethylenemethane is an important synthetic building block in many synthetic transformations.^{3–9} Isotopically labelled compounds of this type may be useful as spectroscopic and mechanistic probes.^{10,11} Herein, we report the syntheses of **1** and its 1,1- d_2 - and 1,1,1',1',3,3- d_6 -isotopomers.

Results and discussion

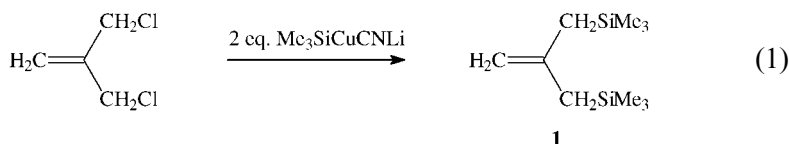
Miginiac reported a straightforward synthesis of **1** by disilylation of isobutene dianion.³ However, we encountered several problems when using this method. First, trace amounts (4–5% by GC-MS) of (*E*)- and (*Z*)-2-trimethylsilylmethyl-1-trimethylsilyl-propenes are produced as by-products in the synthesis. These impurities are very difficult to remove by distillation, and they may produce isomers of trimethylenemethane anion in subsequent gas-phase reactions. In addition, we found a significant amount of deuterium/hydrogen exchange between d_8 -isobutene and the hydrocarbon solvent during dianion formation, which led to about 15% deuterium loss (by mass spectrometry) in the labelled product.

We sought an alternative synthesis of **1** that can also be adapted to synthesize the deuterium labelled compounds, d_2 - and d_6 -**1**, with high isotopic purity. We found that lithium trimethylsilylcyanocuprate readily reacts with commercially available 2-chloromethyl-3-chloro-1-propene to give **1** in excellent yield (Equation (I)).^{12,§} The mild reaction

‡The mass spectrometric nature of these experiments requires complete isomeric purity of the neutral precursors. The limited sensitivity and mass resolving power of the instruments require a few grams of the samples and greater than 98% isotopic incorporation.

§A slightly modified procedure was used. To a solution of hexamethyldisilane (4.0 g, 27.0 mmol) in 16.0 ml hexamethylphosphoramide (HMPA) at 0°C was added dropwise a solution of halogen-free methylolithium (17.0 ml, 1.6 M in ethyl ether, 27.2 mmol). The solution was stirred under nitrogen atmosphere at –5–0°C for 15 min. Then, it was cooled to –50°C and a suspension of copper(I) cyanide (1.7 g, 19.0 mmol) in 50 ml THF was added via a Teflon[®] cannula under nitrogen. The reaction mixture was vigorously stirred at –40 ± 5°C for an hour, then cooled to –78°C, and 3-chloro-2-chloromethyl-1-propene (1.2 ml, neat, 8.9 mmol) was added. The resulting reaction

conditions used for this procedure permitted the efficient syntheses of the deuterium labelled compounds of **1**, as shown in Schemes 1 and 2.

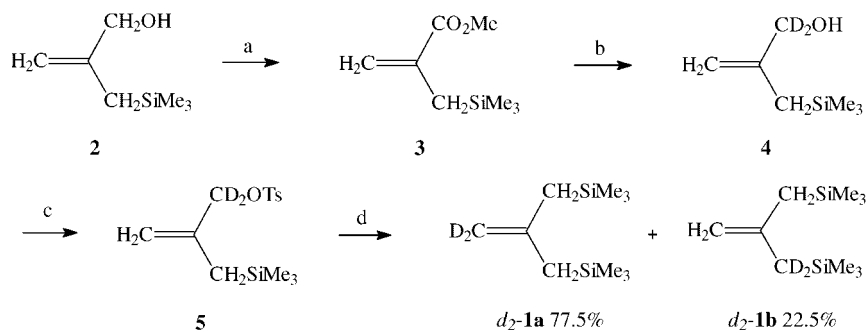


For the synthesis of d_2 -**1**, 2-trimethylsilylmethyl-2-propen-1-ol (**2**)¹³ was first oxidized in two steps with manganese dioxide to methyl 2-trimethylsilylmethylacrylate **3**.¹⁴ Deuterium was then introduced into the molecule by reduction with LiAlD_4 . The product, 1,1- d_2 -2-trimethylsilyl-2-propen-1-ol (**4**), was then converted to the corresponding tosylate **5** and reacted with lithium trimethylsilylcyanocuprate to give the desired product d_2 -**1** in 54% isolated yield. This displacement reaction may proceed through an $\text{S}_{\text{N}}2'$ reaction to give d_2 -**1a** or an $\text{S}_{\text{N}}2$ pathway to give d_2 -**1b**. Similar to the non-deuterated compound **1**, the ^1H -NMR spectrum for d_2 -**1** displays three resonance signals at 0.1, 1.44, and 4.36 ppm, which were assigned, respectively, to the trimethylsilyl-group, allylic, and vinylic hydrogens. The allylic hydrogen peak in the ^1H -NMR of d_2 -**1** is noticeably sharpened compared to that of **1**, due to the smaller vinyl-allylic D–H coupling. Integrations of the peaks at 1.44 and 4.36 ppm gave a ratio of 189/24, which indicated that, the $\text{S}_{\text{N}}2'$ reaction is favored by 3.4 to 1. To our knowledge, this is the first deuterium labelling study that evaluates the competing $\text{S}_{\text{N}}2'$ and $\text{S}_{\text{N}}2$ reactivity of the lithium trimethylsilylcyanocuprate reagent.

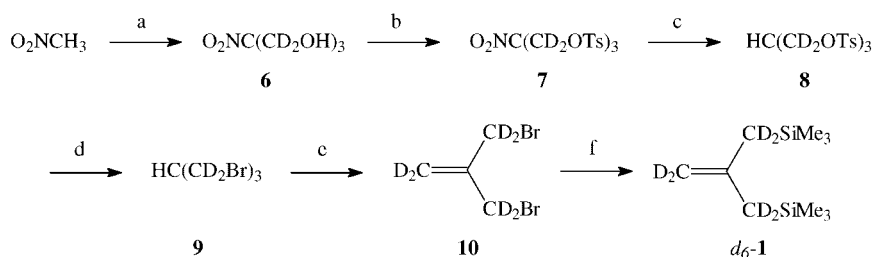
For the synthesis of d_6 -**1**, the deuterium labelled 2-hydroxymethyl-2-nitro-1,3-propanediol (**6**) was obtained from a triple-condensation of commercially available perdeuterated *p*-formaldehyde with nitromethane. The reaction was found to proceed in nearly quantitative yield when carried out in anhydrous ethanol with a catalytic amount of potassium hydroxide (3–5 mol%).¹⁵ Compound **6** was converted under standard conditions to the corresponding d_6 -tris(tosylate) **7**, which was

(footnote continued)

mixture was warmed gradually to room temperature over a period of 2 h and quenched with an aqueous solution of ammonium chloride (40 ml). The aqueous layer was separated and extracted with ethyl ether. The combined organic layers were washed with brine (3×20 ml) and dried with anhydrous sodium sulfate. After removal of the solvent under reduced pressure, the crude product was purified by vacuum distillation to afford 1.5 g (74–76°C/15 Torr, 82% yield) of product as a colorless liquid: ^1H NMR (CDCl_3) δ 0.10 (s, 18H), 1.43 (s, 4H), 4.37 (s, 2H) ppm; ^{13}C NMR (CDCl_3) δ 0.98, 29.94, 130.45, 145.53 ppm; IR (neat): 3086, 2956, 1622, 1420, 1248, 1156, 860, 736 cm^{-1} ; GC-MS (EI) *m/e* (intensity) 73(100.00), 84(13.45), 97(5.92), 112(15.95), 185(5.43), 200(3.85).



Scheme 1. (a) (1) MnO_2 , hexanes; (2) MnO_2 , NaCN, AcOH, MeOH, 73% (b) LiAlD_4 , THF 88%; (c) TsCl, Py, 77%; (d) $\text{Me}_3\text{SiCuCNLi}$, HMPA, THF, 54% total



Scheme 2. (a) $(\text{CD}_2\text{O})_n$, KOH, EtOH, 95%; (b) TsCl, Py, CH_2Cl_2 , 86%; (c). Bu_3SnH , 1,1'-azobis(cyclohexanecarbonitrile), benzene, 92%; (d) LiBr, acetone, 89%; (e) DBU, THF; (f) $\text{Me}_3\text{SiCuCNLi}$, HMPA, THF, 70% from 9

selectively reduced to d_6 -tris(tosylmethyl)methane **8** using tributyltin hydride as the reducing agent.^{16,†} Our original plan was to synthesize 2-(*p*-tosyloxymethyl)allyl tosylate by treating **8** with 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU), and then to carry out double-silylation with the product bis(tosylate). The reaction of **8** with DBU proceeded smoothly even at 0°C in methylene chloride; however, we found the product to be too labile for practical use in the subsequent reaction. Thus, the d_6 -tris(tosylate) **8** was converted to the corresponding d_6 -tribromide **9** by refluxing in acetone with anhydrous lithium bromide.¹⁷ Reaction of d_6 -tris(bromomethyl)methane with DBU in THF produced

[†] A modified procedure was used. A degassed solution of **8**, 1.2 equivalent tributyltin hydride and 0.05 equivalent 1,1'-azobis(cyclohexanecarbonitrile) in benzene was refluxed for 5 h. After removal of solvent under reduced pressure, the solid residue was chromatographed on silica gel to yield the pure product.

*d*₆-2-bromomethyl allylbromide **10**, which, in turn, produced *d*₆-**1** in 70% yield from **9**, upon treatment with lithium trimethylsilylcyanocuprate.^{||}

General procedures

All reactions were conducted under Ar atmospheres and monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E.M. silica gel plates (60F-254) using UV-light detection or 5% anisaldehyde and 5% sulfuric acid as the visualization reagent. E.M. science silica gel 60 (230–400 mesh ASTM) was used for flash column chromatography.

LiAlD₄ (98 at% D) and (CD₂O)_n (99 at% D), were purchased from Aldrich Chemical Co. Other common reagents were also purchased from Aldrich with a few exceptions from other commercial sources. Tetrahydrofuran and benzene were distilled from sodium benzophenone ketyl under Ar. Methylene chloride, hexanes, pyridine and diisopropylamine were distilled from calcium hydride under Ar. Other reagents were purified by literature procedures.¹⁸

¹H and ¹³C NMR spectra were recorded in CDCl₃ or C₆D₆ on a Varian Gemini-200 and a GE QE-300 NMR spectrometers. IR spectra were taken on either a Perkin-Elmer 1310 or a Perkin-Elmer 1600 FT-IR spectrophotometer using sodium chloride plates. GC-MS spectra were taken with a Finnigan 4000 mass spectrometer.

Conclusions

As demonstrated by the above syntheses, the title compounds can be conveniently prepared from the displacement reactions of lithium trimethylsilylcyanocuprate. No detectable isomeric impurities were found and no loss of deuterium was observed in the course of these transformations.

Acknowledgements

This manuscript is dedicated to the memory of Professor Robert R. Squires.

^{||} The compound displays identical TLC and GC behaviors as the non-deuterated **1** and IR (neat): 2956, 2906, 1570, 1248, 968, 910, 842, 736, 690, 650 cm⁻¹; GC-MS (EI) m/e (intensity) 73(100.00), 74(15.45), 103(3.61), 116(4.89), 117(8.31), 118(7.30), 191(8.90), 206(6.08).

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